THE USE OF AI AND ADVANCED COMPUTER SYSTEMS TO DEVELOP DRUGS AGAINST NEW EMERGING THREATS

Next Generation Synthesis Of Therapeutic Drugs Through Computational Design And Embedded Experimental Validation

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Synthetic biology's remarkable potential to provide novel therapeutic drugs is inhibited by very long development times due to our significant limitations in predictably engineering biological systems. Recent advances in Artificial Intelligence, robotics, and synthetic biology open the possibility to provide the predictive power synthetic biology currently needs. We have developed, for example, tools to suggest molecules predicted to have desired properties (e.g. a binding constant of 50 nM), algorithms to recommend DNA designs that encode the biological pathways to synthesize them, semiautomated pipelines to build the strains that harbor these pathways, and machine learning approaches to improve the process based on the experimental results.

We showcase these technologies by synthesizing unnatural lactams using the microbial host Pseudomonas putida and a retrobiosynthesis approach based on polyketide synthases. Lactams are commonly employed directly as monomers for the synthesis of polymers, the most prominent example of which is nylon-6. Polyketide synthases (PKSs) are modular biosynthetic assembly lines responsible for combinatorially diverse natural products in bacteria and fungi. We developed a semiautomated synthesis pipeline able to build hundreds of PKS designs, the first of its kind. We created a retrobiosynthesis algorithm able to recommend DNA designs to obtain a desired target molecule, and we used machine learning to predict which designs are more likely to succeed.

We propose to pivot these experimental and computational tools, so far devoted to replacing fossil fuels and petrochemicals, to synthesize therapeutic molecules. This will enable on-demand synthesis of novel molecules tailored to individual pathologies and patients for precision medicine. As an initial proof of concept, we propose to showcase the use of these technologies to synthesize new antibiotics or antivirals.

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